

CLAIMS

What is claimed is:

1 1. A method of detecting a predisposition to cancer in an animal, said
2 method comprising:
3 (i) providing a biological sample from said animal;
4 (ii) detecting the level of *CYP24* within said biological sample; and
5 (iii) comparing said level of *CYP24* with a level of *CYP24* in a control
6 sample taken from a normal, cancer-free tissue;
7 wherein an increased level of *CYP24* in said biological sample compared to the level of
8 *CYP24* in said control sample indicates a predisposition to cancer in said animal.

1 2. The method of claim 1, wherein said level of *CYP24* is detected by
2 determining the copy number of *CYP24* genes in the cells of said biological sample.

1 3. The method of claim 2, wherein said copy number is measured using
2 Comparative Genomic Hybridization (CGH).

1 4. The method of claim 1, wherein said copy number is determined by
2 hybridization to an array of nucleic acid probes.

1 5. The method of claim 3, wherein said Comparative Genomic
2 Hybridization is performed on an array.

1 6 The method of claim 1, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* mRNA in said biological sample, wherein an increased level
3 of *CYP24* RNA in said sample compared to *CYP24* RNA in said control sample indicates a
4 predisposition to cancer.

1 7. The method of claim 6, wherein said level of *CYP24* mRNA is
2 measured in said biological sample and said control sample at the same vitamin D receptor
3 activity or the *CYP24* mRNA levels are normalized to the level of vitamin D receptor
4 activity in the sample and control.

1 8. The method of claim 6, wherein said level of *CYP24* mRNA is
2 measured by hybridization to one or more probes on an array.

1 9. The method of claim 1, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* protein in said biological sample, wherein an increased level
3 of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample
4 indicates a predisposition to cancer.

1 10. The method of claim 9, wherein the level of *CYP24* protein is
2 measured in the biological sample and the control sample at the same vitamin D receptor
3 activity or the protein levels are normalized to the level of vitamin D receptor activity in the
4 sample and control.

1 11. The method of claim 1, wherein said level of *CYP24* is detected by
2 measuring the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said
3 biological sample, wherein an increased level of 25-hydroxyvitamin D3 24-hydroxylase
4 enzyme activity in said sample as compared to 25-hydroxyvitamin D3 24-hydroxylase
5 enzyme activity in said control sample indicates a predisposition to cancer.

1 12. The method of claim 11, wherein said level of 25-hydroxyvitamin D3
2 24-hydroxylase activity is measured in said biological sample and said control sample at the
3 same vitamin D receptor activity or the activity levels are normalized to the level of vitamin
4 D receptor activity in the sample and control.

1 13. The method of claim 1, wherein said animal is a mammal selected
2 from the group consisting of humans, non-human primates, canines, felines, murines,
3 bovines, equines, porcines, and lagomorphs.

1 14. The method of claim 1, wherein said biological sample is selected
2 from the group consisting of excised tissue, whole blood, serum, plasma, buccal scrape,
3 saliva, cerebrospinal fluid, and urine.

1 15. The method of claim 1, wherein the difference between said increased
2 level of *CYP24* in said biological sample and the level of *CYP24* in said control sample is a
3 statistically significant difference.

1 16. The method of claim 1, wherein said increased level of *CYP24* in said
2 biological sample is at least about 2-fold greater than the level of *CYP24* in said control
3 sample.

1 17. The method of claim 1, wherein said increased level of *CYP24* in said
2 biological sample is at least about 4-fold greater than said level of *CYP24* in said control
3 sample.

1 18. A method of estimating the survival expectancy of an animal with
2 cancer, said method comprising:

- 3 (i) providing a biological sample from said animal;
4 (ii) detecting the level of *CYP24* within said biological sample; and
5 (iii).comparing said level of *CYP24* with the level of *CYP24* in a
6 control sample taken from a normal, cancer-free tissue;
7 wherein an increased level of *CYP24* in said biological sample compared to the level of
8 *CYP24* in said control sample indicates a reduced survival expectancy in said animal
9 compared to in an animal with cancer that has a normal level of *CYP24*.

1 19. The method of claim ~~18~~, wherein said level of *CYP24* is detected by
2 determining the copy number of *CYP24* genes in the cells of said animal.

1 20. The method of claim 19, wherein said copy number is determined by
2 hybridization to an array of nucleic acid probes.

1 21. The method of claim 19, wherein said copy number is measured using
2 Comparative Genomic Hybridization. _____

1 22. The method of claim 21, wherein said Comparative Genomic
2 Hybridization is performed on an array. _____

1 23. The method of claim 18, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* mRNA in said biological sample, wherein an increased level
3 of *CYP24* RNA in said sample as compared to *CYP24* RNA in said control sample indicates
4 a reduced survival expectancy.

1 24. The method of claim 23, wherein said level of *CYP24* mRNA is
2 measured in said biological sample and said control sample at the same vitamin D receptor
3 activity or the activity levels are normalized to the level of vitamin D receptor activity in the
4 sample and control.

1 25. The method of claim 18, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* protein in said biological sample, wherein an increased level
3 of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample, at a
4 given level of vitamin D receptor activity indicates a reduced survival expectancy.

1 26. The method of claim 18, wherein said level of *CYP24* is detected by
2 measuring the level of 25-hydroxyvitamin D₃-24-hydroxylase enzyme activity in said
3 biological sample, wherein an increased level of 25-hydroxyvitamin D₃ 24-hydroxylase
4 enzyme activity in said sample as compared to 25-hydroxyvitamin D₃ 24-hydroxylase
5 enzyme activity in said control sample indicates a reduced survival expectancy.

1 27. The method of claim 26, wherein said level of 25-hydroxyvitamin D₃
2 24-hydroxylase activity is measured in said biological sample and said control sample at the
3 same vitamin D receptor activity or the activity levels are normalized to the level of vitamin
4 D receptor activity in the sample and control.

1 28. The method of claim 18, wherein said animal is a mammal selected
2 from the group consisting of humans, non-human primates, canines, felines, murines,
3 bovines, equines, porcines, and lagomorphs.

1 29. The method of claim 18, wherein said biological sample is selected
2 from the group consisting of excised tissue, whole blood, serum, plasma, buccal scrape,
3 saliva, cerebrospinal fluid, and urine.

1 30. The method of claim 18, wherein the difference between said
2 increased level of *CYP24* in said biological sample and the level of *CYP24* in said control
3 sample is a statistically significant difference.

1 31. The method of claim 18, wherein said increased level of *CYP24* in
2 said biological sample is at least about 2-fold greater than the level of *CYP24* in said control
3 sample.

1 32. The method of claim 18, wherein said increased level of *CYP24* in
2 said biological sample is at least about 4-fold greater than the level of *CYP24* in said control
3 sample.

1 33. A method of treating cancer in an animal, said method comprising:
2 (i) providing a biological sample from said animal;
3 (ii) detecting the level of *CYP24* within said biological sample;
4 (iii) comparing said level of *CYP24* with a level of *CYP24* in a control
5 sample from a normal, cancer-free tissue; and
6 (iv) selecting and performing a cancer therapy in those animals having
7 an increased level of *CYP24* compared to the level of *CYP24* in said control sample.

1 34. The method of claim 33, wherein said cancer therapy is selected from
2 the group consisting of chemotherapy, radiation therapy, surgery, antihormone therapy, and
3 immunotherapy.

1 35. The method of claim 34, wherein said cancer therapy is an adjuvant
2 cancer therapy.

1 36. The method of claim 33, wherein said level of *CYP24* is detected by
2 determining the copy number of *CYP24* genes in the cells of said animal.

1 37. The method of claim 36, wherein said copy number of *CYP24* genes is
2 determined by hybridization to an array of nucleic acid probes.

1 38. The method of claim 36, wherein said copy number of *CYP24* genes is
2 measured using Comparative Genomic Hybridization (CGH).

1 39. The method of claim 26, wherein said Comparative Genomic
2 Hybridization is performed on an array.

1 40. The method of claim 33, wherein said level of *CYP24* is detected by
2 measuring the levels of *CYP24* mRNA in said biological sample, wherein an increased level
3 of *CYP24* RNA in said sample as compared to *CYP24* RNA in said control sample indicates
4 the need for an adjuvant cancer therapy.

1 41. The method of claim 40, wherein said level of *CYP24* RNA is
2 measured in said biological sample and said control sample at the same vitamin D receptor
3 activity or the activity levels are normalized to the level of vitamin D receptor activity in the
4 sample and control.

1 42. The method of claim 33, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* protein in said biological sample, wherein an increased level
3 of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample
4 indicates the need for an adjuvant cancer therapy.

1 43. The method of claim 42, wherein said level of *CYP24* protein activity
2 is measured in said biological sample and said control sample at the same vitamin D receptor
3 activity or the activity levels are normalized to the level of vitamin D receptor activity in the
4 sample and control.

1 44. The method of claim 33, wherein said *CYP24* level is detected by
2 measuring the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said
3 biological sample wherein an increased level of 25-hydroxyvitamin D3 24-hydroxylase
4 enzyme activity in said sample as compared to 25-hydroxyvitamin D3 24-hydroxylase
5 enzyme activity in said control sample, at a given level of vitamin D receptor activity
6 indicates the need for an adjuvant cancer therapy.

1 45. The method of claim 44, wherein said level 25-hydroxyvitamin D3
2 24-hydroxylase enzyme activity is measured in said biological sample and said control
3 sample at the same vitamin D receptor activity or the activity levels are normalized to the
4 level of vitamin D receptor activity in the sample and control.

1 46. The method of claim 33, wherein said animal is a mammal selected
2 from the group consisting of humans, non-human primates, canines, felines, murines,
3 bovines, equines, porcines, and lagomorphs.

1 47. The method of claim 33, wherein said biological sample is selected
2 from the group consisting of excised tissue, whole blood, serum, plasma, cerebrospinal fluid,
3 buccal scrape, saliva, and urine.

1 48. The method of claim 33, wherein the difference between said
2 increased level of *CYP24* in said biological sample and the level of *CYP24* in said control
3 sample is a statistically significant difference.

1 49. The method of claim 33, wherein said increased level of *CYP24* in
2 said biological sample is at least about 2-fold greater than the level of *CYP24* in said control
3 sample.

1 50. The method of claim 33, wherein said increased level of *CYP24* in
2 said biological sample is at least about 4-fold greater than the level of *CYP24* in said control
3 sample.

1 51. A method of screening a test agent for the ability to inhibit
2 proliferation of a *CYP24*-expressing cell, said method comprising:
3 (i) contacting said *CYP24*-expressing cell with said test agent; and
4 (ii) detecting the level of *CYP24* activity;
5 wherein a decreased level of *CYP24* activity as compared to the level of *CYP24* activity in a
6 cell not contacted with said agent indicates that said agent inhibits proliferation of said cell.

1 52. The method of claim 51, wherein said cell is contacted with vitamin
2 D.

1 53. The method of claim 51, wherein said detecting comprises detecting
2 the level of *CYP24* mRNA, wherein a decreased level of *CYP24* mRNA in said *CYP24*-
3 expressing cell as compared to the *CYP24* mRNA level in a cell not contacted with said
4 agent sample, at a given level of vitamin D receptor activity indicates that said agent inhibits
5 proliferation of said cell.

1 54. The method of claim 51, wherein said detecting comprises hybridizing
2 a nucleic acid from said cell to an array of nucleic acid probes.

1 55. The method of claim 51, wherein said detecting comprises detecting
2 the level of *CYP24* protein, wherein a decreased level of *CYP24* protein in said *CYP24*-
3 expressing cell as compared to the *CYP24* protein level in a cell not contacted with said
4 agent sample indicates that said agent inhibits proliferation of said cell.

1 56. The method of claim 55, wherein said level of *CYP24* protein in said
2 contacted cell and said cell not contacted with said agent is measured at the same vitamin D
3 receptor activity or the *CYP24* protein levels are normalized to the level of vitamin D
4 receptor activity in the sample and control.

1 57. The method of claim 51, wherein said detecting comprises detecting
2 the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said cell, wherein an
3 decreased level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said *CYP24*-
4 expressing cell as compared to the 25-hydroxyvitamin D3 24-hydroxylase enzyme activity
5 level in a cell not contacted with said agent sample, at a given level of vitamin D receptor
6 activity indicates that said agent inhibits proliferation of said cell.

1 58. The method of claim 57, wherein said level of 25-hydroxyvitamin D3
2 24-hydroxylase enzyme activity in said contacted cell and said cell not contacted with said
3 agent is measured at the same vitamin D receptor activity or the activity protein levels are
4 normalized to the level of vitamin D receptor activity in the sample and control.

1 59. The method of claim 51, wherein said *CYP24*-expressing cell is a
2 tumor cell.

1 60. The method of claim 51, wherein said *CYP24*-expressing cell is a
2 hyperproliferative cell.

1 61. The method of claim 51, wherein the difference between said
2 decreased level of *CYP24* activity and the level of *CYP24* activity in a cell not contacted
3 with said agent is a statistically significant difference.

1 62. The method of claim 51, wherein said decreased level of *CYP24*
2 activity is at least about 2-fold lower than the level of *CYP24* activity in a cell not contacted
3 with said agent.

1 63. The method of claim 51, wherein said decreased level of *CYP24*
2 activity is at least about 4-fold lower than the level of *CYP24* activity in a cell not contacted
3 with said agent.

1 64. A method of decreasing the proliferation of a cell with an elevated
2 level of *CYP24*, said method comprising reducing the level of *CYP24* activity in said cell —
3 using an inhibitor of *CYP24*.

1 65. The method of claim 64, wherein said method further comprises
2 contacting the cell with vitamin D.

1 66. The method of claim 64, wherein said cell is a tumor cell.

1 67. The method of claim 66, wherein said tumor cell is selected from the
2 group consisting of breast cancer cells, prostate cancer cells, colorectal cancer cells,
3 leukemia cells, lymphomas, lung cancer cells, brain cancer cells, pancreatic cancer cells, and
4 ovarian cancer cells.

1 68. The method of claim 64, wherein said cell is a hyperproliferative cell.

1 69. The method of claim 64, wherein said cell is a metastatic cell.

1 70. The method of claim 64, wherein said inhibitor is selected from the
2 group consisting of antisense oligonucleotides, ribozymes, repressors of *CYP24* gene
3 expression, competitive inhibitors of 25-hydroxyvitamin D3 24-hydroxylase activity, and
4 non-competitive inhibitors of 25-hydroxyvitamin D3 24-hydroxylase activity.